

Art Unit: 1644

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with E. Hanley on 11/19/99.

2. The application has been amended as follows:

Canceled claims 67-68 without prejudice.

In claim 71, line 2, deleted "67, 68,".

Added new claim 72 as follows:

<sup>30</sup>  
~~72~~ The pharmaceutical composition of claim <sup>39</sup>~~31~~, which further comprises at least one additional therapeutic agent.--

3. The following is an examiner's statement of reasons for allowance:

Claims 67-68 have been canceled in this examiner's amendment as containing subject matter that would be inherently duplicated in original claims 12 and 15.

Regarding previously stated 112 rejections, there is no necessity for applicant to deposit a cell line secreting the D2E7 antibody. Since the disclosure shows the VH and VL sequences, one skilled in the art would be able to reproduce this antibody.

Regarding previously cited prior art, the examiner notes Griffiths et al do not teach an anti-TNFalpha antibody having a Koff rate constant or a dissociation constant with the instantly

66

Art Unit: 1644

recited limitations. Applicant's urgings filed 2/9/98 at page 10 have been noted. Therein applicant indicates that Griffith et al teach (Table IV) a dissociation constant ( $K_d$ ) of  $6.4 \times 10$  to the minus 6th molar. The examiner notes that what they teach is an association constant ( $K_a$ ) of  $6.4 \times 10$  to the 6th molar to the minus 1. Since this is the reciprocal of  $K_d$ , the actual  $K_d$  would be ca.  $1.56 \times 10$  to the minus 7th molar, which is still outside of the range encompassed instantly.

The examiner further notes that the teachings of Lewis et al do not pertain to an anti-TNF alpha antibody, and one would not know how much improvement in binding the binding characteristics would be attainable when applying Lewis et al's general method to any particular antibody.

Regarding newly found art, Boyle et al (5,654,407) is cited as of interest. This corresponds to EP 614,984, cited at instant specification page 2, line 12. The instant invention is distinguishable over the US reference for the reasons set forth in the instant specification regarding the EP reference.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. Saunders whose telephone number is (703) 308-3976.

Application/Control Number: 599,226

Page 4

Art Unit: 1644

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, C. Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

DAS

November 19, 1999

*David A. Saunders*  
DAVID SAUNDERS  
PRIMARY EXAMINER  
ART UNIT 182/644